Pigmentary disorders

- Basics

- Color of skin: caused by 4 factors:
  1. Hb — oxyHb → red color; deoxyHb → Blue
  2. Melanin → Brown
  3. Carotenoids: obtained from plant diet — orange, Carrot.

Melanocytes

- Dendritic, Pigment synthesizing Cell that derived from ! Neural Crest & rests bet. KCs at BMZ.
- Embryology: Melanoblast (at Neural Crest) —differed to→ Melanocytes
  → Migrate to:
  - Skin: Epid., dermis & H. Follicle.
  - Inner ear
  - Eye
  - Meninges
- Important Numbers:
  - development at 8 wks IU.
  - Earliest signs of Melanization: 10 wks IU
  - No.: 2×10^9 (Genitalia — Face)
  - No. ↓ by 8% / 10 yr.
  - MCs : KCs ratio = 1 : 9 (1:4 – 1:10)
  - Each MC supplies Melanosomes to 36 KCs (1:9 & 36 KCs)
    by process of Apocopation (Apical part of ! Cell is released Together with the secretory product) [Cytophagocytosis]
- Mic Exam.: by H & E stain: They appear as a Clear Cells at basal cell layer & deeply Stained Nucleus ...

(d.t Artefacts Formed during Fixat° of Specimen That's because MCs lack ⟨ desmosomes & Tonofilaments).

. **DD** from clear spaces of KCs ?? They show ⟨ (all. cell junct° layer of cytoplasm periphery to the Halo.

. **Special Stains:** (كيمياء)

(1) Fontana-Masson (MCs ع خلايا صبغة)

(2) DOPA oxidase react°

(3) Immunohistochemical (Markers) ⟨ S100 / Mart-1 / HMB 45

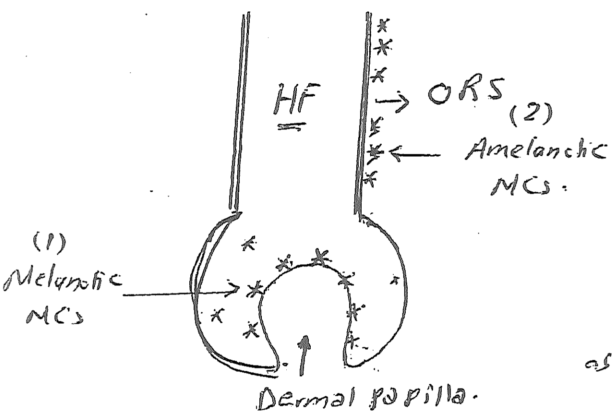
. **NB DOPA oxidase React°:** (تفصيل فكرة تكوين الميلانين)

. Most specific method

. depends on presence of Dopa oxidase (Tyrosinase) enz. inside MCs → so DOPA + skin Biopsy —Tyrosinase→ Melanin product° (Brown-Black deposits).

(أماكن MCs في الجلد) Skin Melanocyte Populations (مهم جدا)

- **Epidermal MCs**
  - موجودة غالبا
  - (Basal bet KCs)



- **Hair follicle MCs**
  - **Melanotic MCs** (DOPA +ve)
    - . interspersed bet. Matrical cells of HF bulb .. Immediately capping the dermal papillae (جذر الشعرة)
    - . وظيفتها: امداد الشعر باللون بتاعه اثناء Anagen
  - **Amelanotic MCs** (DOPA −ve)
    - . Reservior MCs at ORS of HFs.
    - . under NL skin conditions → inactive
    - . under stress (inj. ury, UVL) → prolif. & migrat° to epid. surface → Perifollicular pigmentat° (seen on Vitiligo treated by UVB)

Q1 what the difference bet. Melanotic & Amelanotic MCs of HFs ??

Q2 difference bet. ⟨ epid. MCs & Melanotic MCs of HF → . نشطة باستمرار طوال الحياة / . لا تنشط إلا أثناء فقط (Anagen)

NB . Racial Differences in skin Color is not Caused by differences of MCs Number (both dark & Light skinned show KC : MCs = 9:1)

But This difference is d.t.

(1). Melanosome difference in –
- No
- size
- distribution

(2). Type of Melanin –
- Eumelanin (Brown-black)
- pheomelanin (Red/white)

In Light skin

Melanosomes –
- Fewer
- smaller
- packaged by memb bound Complexes.

In dark skin people

Melanosomes –
- Much larger
- Singly dispersed

Function of Melanocytes

(1) Melanin production –
- Color of skin
- has umbrella like acts over KCs Nucleus → protect them from UVL & so skin Cancer (so lighter skin people أكثر عرضة لسرطانات الجلد)
- Antioxidant → ↓ UVL effect on skin.

(2) MCs: Secrete Cytokines & express cell surface Ag ā suggest their active role in inflammation.

Disadvantage of Melanin

(١) يمتص كمية أشعة شمس وحرارة بنسبة ٣٠٪ أو أكثر من خلايا البشرة فيزيد درجة حرارة الجسم

(٢) يمنع تكوين VitD ← فنشأ كده مرض الكساح ينتشر في الأطفال السمر أكثر

Melanosomes in Different Colors

light skin	Dark skin
. Stage II Melanosomes	. stage III & IV
. Size < 0.5 um	> 0.5 um
No/MC < 20	. > 200
distribute: groups	. disperse (single)
. Degradation: Fast	. slow

Pathway of epidermal melanin pigmentation

(10 steps)

1. Migration of Melanoblasts ⟷ لو حدث خلل → . piebaldism . Waardenburg synd.
↓
2. Differentiate into MCs
↓
3. Mitosis of MCs — خلل → Vitiligo
↓
4. Synthesis of TYR enz. — " → Albinism
↓
5,6,7. Synthesis of Melanosomes → Chediak Higashi / Ash leaf of TSC.
↓
8. Melanosomes Melanization → Albinism / PVC / IGH
↓
9. Melanosome Transfer
↓
10. Melanosome

(9, 10) — اي خلل فيهم → . Chediak H. . Nevus depigment. . PVC . Pit. Alba.

• Melanin Synthesis

. phenylalanine aa
↓ pha Hydroxylase (نقص الانزيم ده → (phenyl ketonuria) (PKU))
Tryosine
↓ (Tyrosinase enz.)
DOPA
↓ (Tyrosinase enz.)
DOPA Quinone
→ Pheomelanin
→ Eumelanin

. Eumelanin	. Pheomelanin
. Ellipsoid melanosomes	. Spherical
. dark (brown-black)	. Contains cysteine.
	. light (yellow or red)

(٤:٥٢) للدكتورة ضحى

Types of Skin Color = NL Pigments

1. Constitutive : Genetically determined
2. Facultative (Inducible) ← UVR / Hormones

Caucasoid → White
Mongoloid → Oriental
Negroid → Black
Australoid → Aboriginal

Control & Regulation of Skin Pigments

(1) Genetic factors (Constitutive)

(2) UVL : ↑ MCs, ↑ Melanosomes, ↑ Tyr. enz activity

(3) Immediate Pigment darkening (IPD) & delayed Tanning (see Light & Skin).

(4) Endocrinal : α-MSH, ACTH, Estrogen.

(5) Biochemical Factors : IL1 α & β, IL 6 & TGFβ

Enzymes & proteins involved in Melanogenesis.

- Tyrosinase enz.
- Tyrosinase Related protein (TRP1 & 2)
- Melanocortin Receptors (MCR1)
- MITF = Microophthalmia associated Transcription Factor → (if Mutat^) → (Waardenburg & Tietz Synd.);

Stages of Melanosomes Development (4)

- Stage I → Spherical No Melanin
- Stage II → oval, great activity of Tyrosinase.
- Stage III : as stage II + moderate deposits of Melanin.
- Stage IV : oval, little activity of Tyr., Much Melanin.

Basics - Melanocytes

قرزة
Mell

NL skin color caused by 4 agents:-

(لون) → Melanin, Hb, Carotenoids

1. **Red** → oxy Hb
2. **Blue** → deoxygenated Hb
3. **Yellow-orange** → exogenous from diet (plant) (**Carotenoids**) → orange, carrot
4. **Brown** → Melanin

Melanocytes

def dendritic, pigment-synthesizing cells that derived from the Neural crest.

Site May be found in:

- skin → Epid, dermis & hair follicle → ORs, Bulb
- Inner ear
- Eye
- Leptomeninges
- around BVs
- around peripheral Ns
- Coelomic cavity

MCs
- mass 1.5 gm, ٢٠١ غرام
- Epid MCs No 2x10⁹ cells
- أكثر في → face, genital
- MCs ↓ by age (8% /10 Ys)
- development 8 Ws IU
- melanizat 10 Ws IU
- MCs 2 Types → secretory: KCs (cytocrine); Non M: KCs لا تفرز

Origin they arise from **Melano blasts** w differentiate to Melanocytes either before or after Migratⁿ from Neural crest.

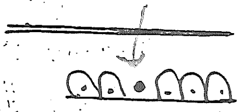
Migratⁿ starts at 2.5 Ws → reach epid at 8 Ws → earliest signs of Melanizat at 10 Ws.

Redistrib. Melanosomes from perinuclear zone to dendrites' origin (Melanophores).

Mic **H&E** → appear as a "clear cell" in basal cell layer (with) dark staining Nucleus. The apparent halo is def artefact formed during fixatⁿ of specimen. This is because

xx Melanocytes lack — desmosomes & — Tonofilaments

Small clear, deeply stained Nuc



DD from clear spaces of KC: they show — Cell-Cell — Layer of Ey peripheral ...

Special Stain:-
- DoPA oxidase Reaction
- Silver stain (Warthin-Starry)
- Immunohistochemical ← S-100, HMB-45, Mart-1 → Silver

HL

EIM:
- No desmosomes or Tonofilaments
- **Nucleus:** Rounded or Oval & double memb., the outer is Rough & separated from the inner by clear Zone.
- **Nucleolus:** Warm-like made up of Loads of Small dense particles out a Limiting memb.
- **Cytoplasm:** Contains:
  - Mitochondria (Num.)
  - MiCrs & interm. Filaments
  - MiCrs tubules
  - Abundant SER & rER
  - Golgi
- Several Mobile dendritic processes extend from each Melanocyte bet epid. Cells

Melanocyte Population

Epidermal (Epidermal Melanin Unit)

1- at basal Cell layer, Just above the BM

2- Ratio of MCs : basal KCs (1:4 - 1:10) (1:10 الأكثر)

3- each Single MC supply 36 KCs. give it

4- Melanosomes by Process of (Apocopation) = Apical part of the Cells is released together the secretory products.

Follicular

at hair bulb immediately Capping the dermal papillae (DP)

1- Supplying melanin to growing epith. Cells of hair Shaft.

2- Giving hair its Color.

at outer Root sheath (ORS) act as a Reservoir

outer Root sheath MCs

- (Dopa +ve) → Melanotic MCs → at lower portion of hair Follicle.
- Amelanotic MC (Dopa -ve) → at upper portion mainly at infundibulum

- the Amelanotic MCs: prolif. & migrate upward & start actively synthesing melanin at the infundibulum → migrate to epid surface. When (work under x stress) → skin exposed injury or stimulated by UVL

NB
- the outer Root sheath MCs represent Resvior MC ŵ are stimulated by PUVA to Repigment Vitiliginous Patches → Perifollicular Pigm.

⊙ Distribut°:-

- in NL Sunprotected skin: (MC: KC) = (1:4 or 1:10)
- Face, shins, Genitalia → higher No of MCs
- in heavily, Sundamaged, facial skin: KC:MC = 1:1
- Racial differences in skin Colour (not) Caused by by differences of MCs No but d.t:-
  - No
  - Size
  - distribut°
  - Type.
  1. No, size & distribut° of Melanosomes.
  2. Pigment grs ēin KCs.

⊙ Pale skin → Few melanosomes that are Smaller & Packaged ēin memb-bound Complexes.

⊙ dark skin → Much melanosomes that are Large & Singly dispersed.

- Function of Melanocytes
  1. Melanin synth → skin color ↔ protect° of lower Skin layers From UVL
  2. Melanin: act as scavenger for metal Ions & Free Radicals (From Cell Metabolism or UVR exp.)
  3. MC → secrete cytokines & express Cell Surface Ag ŵ suggest their active Role in inflammatory react

Epid. Hyperpigmentat° (Melanoc

* Melanocytic (↑ No of MCs)

- Lentigenes.
- Peutz-Jegher Synd.
- PUVA
- Melanocytic Nevi
- MM

Lentigenus

- Nevi

* Melanotic (↑ Melanin)

- Freckles
- Melasma
- CALM
  - Becker's Melanosis
  - Nevus-spilus
- Fanconi Anemia
- Dyskeratosis Congenita
- Ip

Endocrinal

- Cushing
- Addison
- Acromegaly
- Hyperthyroidism
- Pheochromocytoma
- pregnancy
- OCPs.
- ⊙ ACTH ↑↑

Systemic Causes

- RF
- LCF
- ⊙ Hemochromatosis
- ⊙ Amyloidosis

3N

- Infect
- AICTDs
- Neoplastic
- Neurological
- Nutritional:
  - Anemia
  - pellagra
  - Vit A def.
  - malabsorpt°.

Drugs

- Phytophoto
- Berloque
- EDP
- Civatte Poikil
- Erythrose
- peribuccale pigmentaire

• Epidermal Melanocytic Hyperpigm

• Lentigo (Lentigines)
المفرد — الجمع

• def :. Small, Pigmented, Flat or Slightly raised spot ē well defined edge. hav. ↓:
brown - dark brown or black color

① Site < Skin / MM < sun exposed / sun protected (Genitles)

② Histologically: ↑ Mcs No & activity

عشان نفرق بين Freckles are:-
- Sunexposed
- No mm Lighter < lentigenes.
- Melanotic

• Types of Lentigo < lentigenes / lentigenesis

① Lentigo simplex:-
- Commonest
- at birth or Early childhood.
- XX not ass. ē sunexposure or any medical conditions.

Site: skin, oral, Genital, Nail

② Solar Lentigo: (Brown or Liver Spots)
- at sunexposed, not ass. ē diseases.
- DD: freckles (improved by ✗sun but not lentigo)

③ Ink Spot Lentigo: (Reticulated black solar lentigo)
- Black one among solar ones.

④ PUVA Lentigo: d.t PUVA ##

⑤ Radiation ↓: d.t Radiation

⑥ Tanning bed Lentigo.

⑦ oral & Labial - vulval & Penile Lentigo.

⑧ Generalized = Eruptive = lentiginosis profusa

⑨ Aggminated Lentiginosis / Zostriform / Partial Unilat. (PUL)
- Segmental, stop at middle line
- ± ass. ē diseases

⑩ Inherited ; AD ✓

⑪ Syndrome Associated: (HL)

ⓐ Xeroderma pigmentosum (XP)

ⓑ LEOPARD synd
- L = lentigenes
- E = Electrocardiac Conduction defect.
- O = ocular Hypertelorism = ↑ distance bet. the 2 corners of pupils of Eye.
- P = Pulmonary stenosis
- A = Abnormalities of Genitalia
- R = Retarded growth
- D = Deafness.

ⓒ Peutz-Jeghers Synd ✓

① Lentigenes
- ① perioral → oral & perioral
- ② oral: persistent → Eye & Nose. Hands, feet, fingers, Toes ano genitale.

② Intest. Polyps (Bg Hamartomas)
- Small intestine (sp. Jejunum).
- Risk of intussusception & Mg.
- Abd. pain & bleeding
- Other Types of Mg ± (Sol.)

AD
Mutation in Serine Threonine kinase
chr. 19 p13.3

Rarely → Polyps absent

Invs: Barium & endoscopy 12 y.s

- Lentigenes any where but Commonest at lower lip + dorsum of Hand
- Polyposis any where in GIT but → Commonest at: Jejunum.

(C,D) 2 other Syndromes Related to PJS

Harmless Synd:

Laguier Hunziker Synd.

1- Lentigines:
- sp. at < lower lip, Buccal Cavity
- others: Tongue, fingers, Genitals.

Pigm. may be macular (or) diffuse (as Addison)

2- Pigmented Nail
- streaks (or even half or Total Nail)

3- No intestinal Polyps

Cronkhite Canada Synd:

Pigm 1- Lentigines at: fingers, extremities (no mm)
- pigm. = diffuse (Palmar fingers) / macular (dorsal Hand & Limbs)
- + diffuse pigm. of palmar fingers.

2. Intestinal Polyps (??Mg) (Adenomatous) → 10%

3- Hair loss

4- Nail changes:- thinning, Splitting & Separation.

5- diarrhoea

(Et) protein loosing Enteropathy → Malabs → Hyper pigm-

(HL) Malabs. HH → (↓) pigm.

(E) MYxoma Syndromes = (Carney Complex)

(Syndromes = Atrial Myxomas + Lentigines)

NB. Myxoma = Tm of primitive CT or Tm of CT e⁻ Mexoid (Mucoid) background → Commonest site is Heart.

They are 3

(1) LAMB

- Lentigines: Lip, face, sclera.
- Atrial MYxomas.
- MucoCut " : Breast, Shoulder Tongue.
- Blue Nevi:

(2) NAME Syndrome

- Nevi
- Atrial Myxoma
- Myxoid NF
- Ephelides.

(NB) Carney Complex/Synd: (LAMB: Lentigenes) (NAME: freckles)

Ephelides = freckles = Ephilis

(i) AD
(ii) Melano Cortin -1 R Gene Mutate
(iii) Common in: Fair skin, red / Blond Hair Individ.

Well defined brown Hyperpigm. macules < 0.5 cm in diameter
usually at sun exposed areas ✓

AET

Isolated finding
Not ass. ē any systemic disorders.

ass. ē other disorders

① NAME synd:
- N = Nevi
- A = atrial myxoma
- M = myxoid Neurofibromata
- E = Ephelides

Crowes sign → ② Axillary freckling (NF1) ✓

③ Freckle "like" pigm. seen in XP, Moynahans syn & Drageria

Melasma* ⊕ (Greek *melas* = black)

It is a relatively common acquired, symmetric hypermelanosis characterized by irregular light to gray-brown macules (Fig. 9-11), see also Regional Dermatology, Vol I, Fig. 61.

Sites: There is a predilection for sun-exposed areas, mainly the cheeks (malar prominences), forehead, upper lip, nose and chin.

It is most commonly observed in women in child-bearing age with dark complexion (skin types IV and V) but it has been reported in males in 10% of cases.

(3) **Clinical patterns**

1. Centrofacial pattern. ✓
2. Malar pattern. ✓
3. Mandibular pattern. ✓

- Types Acc to
  - (1) clinical (3) ← Centrofacial, Malar, Mandib
  - (2) Path. (3)
  - (3) W.L (4)

Histopathology

1. Epidermal: ↑ melanin in basal, suprabasal and st. corneum layers.
2. Dermal type: preponderance of melanophages in the superficial and deep dermis.
3. Mixed type: studies suggest an increase in the number and activity of melanocytes.

(4) 3 TYPES are known according to Wood's light examination, *Epidermal* (light-brown), *Dermal* (bluish-grey), or *Mixed* (dark-brown). On examination with Wood's light, epidermal melasma is accentuated but dermal melasma is not. In the mixed type, it enhances the contrast of lesions in some areas and does not in others. In patients with dark complexions (Type VI), Wood's light examination is of no benefit *(inapparent type)*.

Etiological factors

1. Pregnancy
2. Oral contraceptives
3. Endocrine dysfunction (thyroid dysfunction)
4. Genetic factors
5. Racial factors
6. Sunlight
7. Medications (phenytoin)
8. Cosmetics

Of all these factors, genetic and sunlight exposure are the most important.

B: Melasma like pigm ?? Hydantoin

Treatment

I) Daily application of sunscreens: with SPF > 30, e.g. Spectraban®, Photoderm® Max.

Successful treatment of melasma involves the triad of sun-blocks, bleach & time (at least 6 months).

II) Bleaching preparations

1. Hydroquinone (HQ) 2-4% containing creams [Eldoquine® 2%, Eldoquine forte® 4%, Quinocid®, Leucodinin®, Eldopaque® 2-4% (HQ + Sunscreen)]. It is topical tyrosinase inhibitor. Higher concentration should be avoided as it may carry the risk of contact dermatitis, erythema or leukoderma.
2. Tretinoin gel, 0.05% (Retin A®) alone or with hydroquinone.
3. Azelaic acid 20% (Skinoren®): It is a naturally occurring saturated dicarboxylic acid that has demonstrated beneficial therapeutic effects in the treatment of acne and cutaneous hyperpigmentary disorders, e.g. melasma and lentigo maligna. It may arrest the progression of cutaneous malignant melanoma.
   It appears to have selective effects on hyperactive and abnormal melanocytes. There are minimal effects on normally pigmented human skin, freckles, senile lentigines and nevi. The cytotoxic and antiproliferative effects of azelaic acid may be mediated via inhibition of mitochondrial oxidoreductase activity and DNA synthesis. Disturbance of tyrosinase synthesis by azelaic acid may also influence its therapeutic effects.
   Azelaic acid + tretinoin proved to be more effective than Azelaic acid alone and superior to hydroquinone.
4. Kojic acid 2-4%: it acts by chelation of copper essential for tyrosinase. It is less effective than HQ.
5. N-acetyl-4-S-cyste aminyl phenol.
6. Combined preparations:
   - Hydroquinone 2% + Glycolic acid 10% (MD forté bleaching gel®, Neostrata skin lightening®). Kojic acid 2% has been added in some of these combinations.
   - Kligman's formula:
     - Hydroquinone 2-4% (or Kojic acid 2-4%)
     - Tretinoin 0.05%
     - Ascorbic acid (Vit. C) 1%
     - Dexamethasone 0.1%, or Betamethasone 0.05%

Avoid the use of monobenzyl-ether of hydroquinone as it may lead to permanent leukoderma.

7. Chemical peeling (to remove melanin): by Trichloroacetic acid 30-35%, Jessner's solution + TCA 30% or Glycolic acid (50-70%).
8. Q-switched ruby laser is not effective.

Dermal melasma does not respond to the above formulation; cover-up with opaque cosmetics is the only management option.

Becker's Nevus (Melanosis)

- **Onset**: childhood or Adolescence (?? possible Role of Androgen)
- **Clp**: unilat. macule ch By ← Hyperpigm, Hypertrichosis, Hamartoma of Sm.
- usually at: shoulder, Mammary, Scapula, Extremities

Becker's Nevus Synd.

↑ Overgrowth of:

1. Underlying smooth muscles (smoth. ms. hamartoma)
2. adrenal glands.
3. Limb, Fingers.
4. scrotum

(underlying ⁄⁄)

↓ Hypoplasia of: (under growth)

- Breast
- pectoral ms.
- Chest Wall, Spine

(##) → 1- No effective ## (Even Laser) ... ?? Q switched, Erbium, Alex.

2- Treat by → Sun protection, Laser hair Removal, Acne ##.

D.D → Albrights Synd (since birth, CALM+ others)

Giant Hairy Nevus (since birth, dark).

Nevus spilus (Speckled lentigenous Nevus)

الخلفية

CALM studied ē Hyperpigmented Papules & macules (Junctional & Compound Nevi) (or) with Lentigenes.

Path. → CALM Background → melanotic Hyperpigm.

→ dark spots & papules → as Junctional & Compound Nevi

1- Cushing

- pigmentation similar to that of Addison d.t ↑↑ ACTH & β MSH in 10% of Cases

2. Addison's

- Hypofunction of Adrenal gland d.t either (Autoimmune or TB)
  → ↓ Cortisol → ↑ ACTH & β.MSH
- S&S of Addison's

[1] General: weakness, fatigue, w.t Loss, Vomiting & Abd pain (FAHM)

[2] Cut: Generalized Hyper pigm. (Brown)

- اماكن محزة — skin / MM
- Sun or light exposed areas
- Flexures
- Friction & pressure areas
- Creases of Palms & Soles
- surgical scars.
- Nipple, Gums & Genitalias (MM)

Acromegaly / pheochromocytoma: Addison's like

Hyperthyroidism: Many Patterns:-

- Addisonian
- Jellinik's Sign: ↑ Eyelids pigm → جفونه غامقة
- Melasma.
- Vitiligo.

pregnancy & OCPs → Melasma.

ACTH ↑↑ → as Cushing or Addisons

RF	. Facial & palmoplantar diffuse Brown Pigm. d.t ↑ MSH .
LCF Hemochroma-tosis	Hemochromatosis : AR ; affect ← liver, Heart, Endocrinal gl . Hyperpigm. (Bronze, blue gray or brown black) d.t excess Melanin & hemosiderin deposition. usually on sun exposed areas. . Resemble that of Addison, but ± Ass. ē other Cut. signs as: & systemic as: s. Porphyria. - DM - Testic. Failure. . Ichthyosis. - Hepatomegaly . Alopecia. - Cardiomyopathy. . Nail changes. Diagnosis ① ferritin ② HFE gene ③ MRI of Heart & liver
Amyloidosis	→ Macular & papular Types
Inf	Kalazar, Malaria, TB & SBE.
Neoplastic	(1-) Bronchogenic carcinoma → ACTH (2-) Adenocarcinoma → A.N (3-) Lymphoma : (i) Addisons like ē ← Hodgkins & Leukemia. (ii) Diffuse, progressive pigm. ē MF. (iii) Cytotoxic drugs
Nutritional	① Anemia : d.t deficiency of Vit. B12 → Mottled pigm. of Acral areas. (ii) pellagra (iii) Vit. A deficiency : Xerosis + pigm. (iv) Malabsorpt : Addison's like but ē out MM affect
Neurological	- Hepatolenticular degenerat, stress, schizophrenia, - Parkinsonism.

• Other types of Hyperpigm.

(1-) Drug Induced:

. Mechanism →
- ↑ melanin synth → OCPs
- Depositⁿ of drug → phenothiazines & Imipramine
- Non-specific → FDE.

. Most Common Drugs:-

- OCPs.
- phenothiazines (sp chlorpromazine)
- Hydantoin → شبيه جداً بالكلف
- Antimalarial → (See AICTDs).
- Anti-Tm agents:-
  - . localized skin pigm → 5FU
  - . Nail pigm → 5FU, Bleomycin & busulfan.
  - . Teeth → cyclophosph. & Tetracyclines.
  - . Hair → MTX.

(2) Riehl's Melanosis: (pigmented CD)

. Diffuse or Reticulate, dark brown, slate-gray or Blue-Brown pigm. affects the face, Neck & ± Trunk after Contact ē
- Tar
- cosmetic + UVL
- perfumes.

sp. < forehead, Temples

البرفان / المكياج

(3) Erythrose peribuccale Pigmentaire de Brocq:-

- red-Brown pigmentatⁿ develops around the mouth but spares a narrow perioral rim عكس كلف عادي

- usually affect middle age female d.t photodynamic substances in Cosmetics السن

. DD: PIH of perioral dermatitis/or ECZ.

Cerulo derma

(Blue dermal Hyperpigm.) (Blue d.t Tyndall effect)

Melanotic

- FDE.
- Post inflamm.
- Hemochromatosis
- Amyloidosis
- Melasma (dermal).
- Erythema dyschromicum (EDP)
- Erythema ab Igne.
- InContinentia pigmenti.

Melanocytotic (5)

- Mongolian spot
- Nevus of Ota
- N of Ito
- Melanoma Metastases.
- Blue Nevi

Non melanin dermal Pigm.

- Alkaptonuria
- ochronosis, Hemochromatosis
- Drugs:
  - Minocycline, Clofazimine.
  - Antimalarials
  - CPS
  - Gold
  - silver
  - Arsenic.
  - phenothiazines

Bleaching Creams DNNZ.

(1) Hydroquinone

(2) Topical Retinoids: ↑melanin loss by ↑ epid. Turnover; ↓ Contact bet. Kcs & MCs → ↓ melanosome Transfer.

(3) Botanicals
- plant derived
- -- Tyrosinase
- No toxicity
- Arbutin 1% (Glycosylated HQ) (Bact flora ↓↓ HQ)
- glabridin 0.5% (licorice)
- Genetisic acid
- Niacinamide → -- Melanosome Transfer.
- Hesperidine
- Polyphenols.

(4) others:
- Azelaic acid 20%
- Kojic acid (produced by fungus, 1-4%, ± → CD) -- Tyr. Anti-oxidant.
- Mequinol (5-20%)
- N-Acetyl-4 cysteaminylphenol
- N-Acetyl Glucosamin
- Vit C -- TYR. enz.

(5) Topical Cs (Mechanism)
- Initial Bleaching d.t VC
- ↓ Cell Turnover → ↓ active MCs
- ↓ product of precursor steriod Hs → ↓ MSH
- Antip GsR Antileukotriene → -- Melanin.

Facial hyperpigmentation (Melanosis)

سؤال امتحان

1- Melasma
2- Erythema dyschromicum perstans (EDP)
3- Lichen planus pigmentosus (LPP) DD L.P — Et: Cosmetics, Dyes. Face, Flexures only. No papular lesions, No MM. 30% ass. ē classical L.P
4- Riehl's melanosis (RM)
5- Erythromelanosis peribuccale pigmentaire of Brocq (EPP)
6- Poikiloderma of Civatte
7- Erythromelanosis follicularis of face and neck.
8- Nevus of Ota
9- Miscellaneous causes

⊙ Risk pts: Genetic / Racial: dark skin individuals sp. oriental
UVL exposure
photosensitizers: in Cosmetics.

Types of Hyperpigm: clinically, HP, Wood's (See Melasma).

Miscellaneous causes:-

① periorbital Hyperpigm. (Dark Circles) ??

pigm. demarcal lines:
⊙ Familial (AD)
⊙ PDL (Futcher's or Voigt's lines)
⊙ PIH (CD or AD)
⊙ shadowing from: lax skin, Infraorbital swelling

② pseudo chromosis

③ AN → (Acanthosis Nigricans)

###

① Sunprotect
② Avoid Cosmetics ē photodynamic Allergens.
③ Bleaching creams.
④ chemical Peels
⑤ laser.

Hypo Pigmented disorders

DD of Hypopigmented Macule ?? سؤال امتحان

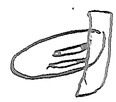
Some definitions:

- **Leukoderma & Hypopigmentation:** Generic non specific terms used to refers to disorders ch. By Lightening of Skin.
- **Hypomelanosis (↓↓):** more specific term means (↓↓) in NL melanin pigmentation.
- **Amelanosis:** total lack of Melanin. (Albinism) — مش موجود من الأول
- **Depigmentat^n^:** Loss of previously existing melanin (Vitiligo) — فقدان الموجود
- **Pigmentary dilution:** (Generalized) lightening of Skin & Hair. e.g (Albinism)
- **Poliosis:** localized whitening of Hair.
- **Canities:** Generalized " " ".

Classification (See [illegible] LP)

[illegible] سؤال مهم

- **Melanopenic** → أشهرهم
  - Albinism
  - Chediak Higashi
  - PKU
  - IGH
  - Progressive Macular Hypomelanosis
- **Melanocytopenic** → أشهرهم
  - Vitiligo
- **Non Melanotic**
  - Nevus anemicus (diascopy; يختفي edge)
  - Anemia
  - oedema.



Albinism

Ⓐ Def: group of genetic disorders ch BY "diffuse" Pigmentary dilution d.t Partial (or) Total Absence of Melanin pigment in MCs of ← skin, Hair, Eyes. [NL No of MCs]

Ⓑ Albinism may affect ← Eye: ocular Albinism (OA)
skin only: Albinoidism
skin + Eye: oculo Cut " (OCA)

Ⓒ Inheritance ← OA → xLR or AR
OCA → AR

- A + MTAP Mutat
- as OCA2 but ↓ variabilty in pigm.
- Common in Japan.
- OCA4

C/P ① Cut. Manifs: ↓ color of skin & Hair → Easy Burning & Cancer

② ocular Manifs: photophobia, Nystagmus, Squint strabismus, ↓ Visual Acuity

Types

- Complete sun avoidance

OCA1 (Tyrosinase Related)
- defectin Tyrosinase (TYR) enz. either
  - Inactive or Absent → OCA1A [called TYR Negative Albinism]
    - less common
    - severe
    - skin pink
    - hair white
  - Partially active (more common) → OCA1B [TYR Positive]
    - More Common
    - less severe

OCA2 (P-Gene related)
- defect in P (Pinked eye) gene on chromosome 15
- less severe than OCA1

OCA3
- defect in TRP1 (Tyrosinase Related protein)
- red hair & skin
- Blue or Brown Eye.

defect
- OCA1: → TYR Enz either
- OCA2: → P gene
- OCA3: → TRP1
- OCA4: → MTAP

disorders of:

Albinism ← Tyrosine

Melanocyte development

Failed differentiation or Migration of Melanoblasts

1. Piebaldism
2. Waardenburg Synd.
   - (See Vitiligo)

• Melanosome Biosynth.

- ⊙ Hermansky-Pudlak Synd
- ⊙ Chediak Higashi Synd.
  - (See below)

Melanosome Transport to KCs

(melanin-clumps in hair & skin)

- Griscelli Synd.
- Chediak Higashi
- others: Pit. Alba, IVC, Nevus depigm, Tub sclerosis

• Hermansky-Pudlak Synd.

هيرمنسكي لوديلاك

(AR) → (8) Types (1-3 ﻣﻬﻤﺔ)

1. Pigmentary dilutn — skin, Hair, Eye — Ocular manifs similar to OCA)
2. Bleeding Tendency ē — NL Platelet Count & ↑↑ Bleeding Time (BT)
3. Pulmonary Fibrosis
4. Granuloma

/. Average life span (30-50)ys

• NB: **Guttate leukoderma:-**

- IGH
- Vitiligo
- LS
- Arsenic
- Confetti like — Tsc, HQ
- planewart (Achromic)
- PVC
- PLC
- PUVA

• **Diseases ē diffuse / Generalized pigmentary dilution**

- ⊙ Albinism
- ⊙ Hermansky Pudlak
- ⊙ chediak Higashi
- ⊙ PKU
- ⊙ Histidinemia
- ⊙ Homocysteinuria

Chediak - Higashi Synd (AR)

- Pigmentary dilution (d.t Macromelanosomes)
  - Pancytopenia.
  - P.N.
  - Pyogenic Recurrent inf. (staph.) < Cut. & sinopulmonary

Macro Melanosomes

HIP

- Granulocytes ē Macro lysosomal grs (giant) → defective phagocytosis → inf.
- Lymphohistiocytes infiltrates of < L.N, spleen, Liver (RES)

☞ ⊙ Death before 20 Ys.

Phenyl Ketonuria (PKU) (AR)

- See diagram of melanin synth.
- deficiency of phenylalanin Hydroxylase enz (ph A)

2 events

↑ phenylalanin level in Blood → ↑ phenylalanine Metabolites < phenyl Pyruvate, phenyl acetat in serum & urine

ph A → tyrosine → (tyrosinase) → Dopa → Dopa q → Eumelanin, pheomelanin

ⓐ Competitive Inhibition of Tyrosinase

ⓑ ↓ Conversion To Tyrosine

→ "Cutaneous pigm dilution"

C/P of PKU

• Cut.

- Oculo Cut. pigmentary dilution
  - Fair Skin
  - Blond Hair
  - Blue Eye.
- Atopic like ECZ
- Scleroderma like lesions (Pseudo scleroderma).
- (4) Bromhidrosis → offensive odour of sweat

• CNS

- (I) MR
- (II) Seizures
- (III) Hypereflexia

• Skeletal

- Microcephaly
- Epicanthus → Skin fold of upper Eye-lid cover inner corner of Eye
- Syndactyly

• Diagnosis

1. ↑↑ Serum phenylalanine level ≥ 15 mg/100mL (Diagnosis)
2. Early diagnosis in Infancy: (Ph.A. level ± NL)

Urine + 5% ferric chloride → green discoloration (d.t ↑ ph. pyruvate level)

أسود ochronosis
أحمر porphyria

TTT (q.Med): Diet low in ph. Alanine; if started early → prevent MR (Not the Cut. Manifs).

NB: 3 Inherited disorders of aa. Metabolism that ± ass. ē Melanopenic Hypomelanosis

(٣ أورار AA +)

1. **PKU**: → defective metabolism of phenylalanine
2. **Histidinemia**: → defective Histidine.
   - Hypopigm.
   - MR
3. **Homocysteinuria**: defective Methionine
   - Hypopigm. – CNS & skeletal
   - Thrombembolism.

Progressive Macular Hypomelanosis:

- Common in young women (18-25) residing in Tropical climates
- C/P → Asymptomatic, ill defined, Nummulars non scaly, Hypopigmented macules & patches on the Trunk ē Rare affection of proximal Ext & Face.
- MF → Buttocks لوزلت
- TVC شكل بالضبط → usually misdiagnosed & Treated as TVC

ttt:-
Topical Clindamycin + Benzyl Peroxide + UVA

- **Histopath.:**
  - ↓ melanin
  - E/M: < uninvolved skin: Large melanosomes; involved skin: small melanosomes bound to memb.
- **AET:** unknown; ± d.t P. Acnes

Idiopathic Guttate Hypomelanosis (IGH)

Acq. leukoderma ch by:- [0.5 - 5 mm pin sized

- Age 40-70 ys
- usually females or
- usually darker skin patients
- chic sites: shin & extensor of forearms.

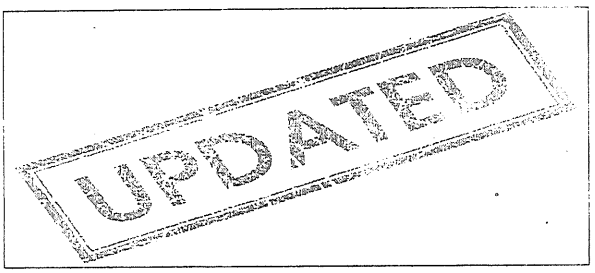
C/P → 0.5 - 5 mm well defined, Percelain white macules ē smooth (Not atrophic surface)

- No < Coalescence. Spont. Resolut.
- Vellous hair in lesions usually retain its pigment.

ttt → No consistently effective ttt; availables ±:

1. ILs ✓ Reasurrance
2. Cryo (in 1 study complete repigm. in 90)
3. Minigrafts مش بلاقه
4. sun protection ...

Sunlight يقتبانه السبب



Vitiligo

Dr.Hany Abo Alwafa

(2015)

VITILIGO

Vitiligo is a common, idiopathic, acquired, circumscribed hypomelanotic/amelanotic skin disorder caused by inactivation or destruction of melanocytes in epidermis and hair follicle and characterized clinically by milky white patches of different sizes and shapes (depig)

- **EPIDEMIOLOGY:** Incidence: 1-2% of general populations, Age: any age, but 50% of cases occur before 20, Sex : M=F — Congenital vitiligo is rare (1%)
- **ETIOPATHOGENESIS**: (Still unknown): "6 theories"

(1) **Genetic theory**: inheritance is polygeneic, 10-20% of cases show +Ve FH. (XX MCs)

(2) **Autoimmune theory:** Evidence: frequent co-occurrence of autoimmune diseases in these patients and their relatives, such as SLE, psoriasis, AA, halo nevi and mainly autoimmune thyroid diseases, besides the favorable response to immunosuppressive therapies (بتحصل مع امراض اخرى)

HI
Igs → TRP1&2 ← *1- Humeral immunity*: Antibodies against melanocyte antigens (Tyrosinase, tyrosinase-related proteins 1 and 2;TRP1,2) → MCs destruction.

↑CD8 / ↓Treg — CMI — *2- Cell mediated immunity*: The high frequencies of melanocyte-reactive cytotoxic T cells ($CD8^+$) in the peripheral blood of patients with vitiligo, perilesional T-cell infiltration and melanocyte loss

- Decreased regulatory T cells activity (Tregs, maintain peripheral tolerance through the active suppression of self-reactive T-cell activation and proliferation). (عشان ما يهاجمش نفسه)

(3) **Neural Theory:** Segmental vitiligo often occurs in a dermatomal pattern. This observation led to a neural hypothesis that proposes that melanocyte destruction in vitiligo is caused directly or indirectly by an inappropriate reaction of the melanocytes to certain neurochemical mediators as neuropeptides, catecholamines or their metabolites, that is secreted from nearby nerve endings.

(4) **Autocytotoxic (Self-destruct) theory:** Toxic metabolites, either from environmental exposures, such as phenol or quinones, or from intrinsic melanin synthesis pathways, may accumulate and damage melanocytes of genetically susceptible individuals. (Ext / Int)

(5) **Oxidative theory:** Accumulation of free radicals toxic to melanocytes (as hydrogen peroxide: H_2O_2) together with decreased level of antioxidant enzymes as catalase, superoxide dismutase, & glutathione peroxidase → oxidative stress →MCs destruction. (↑oxidants (ROS) / ↓Antioxidants — ROS)

(6) **Adhesion defect (melanocytorrhagy) theory**

The main clinical sign reinforcing this theory is the occurrence of koebnerization or Köebner phenomenon It has been suggested that adhesion defects

are involved in the disappearance of melanocytes in vitiligo lesions. Mechanical Trauma → MCs detachment & transepidermal loss.

➢ **Convergence Hypothesis :** Loss of melanocytes in vitiligo appears to occur through a combination of several mechanisms that act in concert.

❖ CLINICAL FEATURES

The most common form of vitiligo is a totally amelanotic macule (or patch) surrounded by normal skin. The color is usually uniformly milk- or chalk-white. Usually, vitiligo is asymptomatic, but occasionally the involved skin may be pruritic.

Although may occur anywhere on the body, there are characteristic patterns of involvement. The most common sites of involvement are areas subjected to repeated trauma or pressure (Koebner) such as elbows, knees, digits, flexor wrists, dorsal ankles and shins, as well as sites of repeated friction such as the body folds (i.e. the axillae, anogenital area). Typically, facial vitiligo occurs around the eyes and mouth (i.e. periorificial). In acrofacial vitiligo, periungual involvement of one or more digits may be associated with lip depigmentation; however, the latter can be an isolated finding.

Hair is usually spared and remain pigmented, but in some cases hair depigmentation (leukotrichia) may also occur simultaneously. In the scalp, vitiligo usually leads to localized patches of grey or white hair, but total depigmentation of the scalp hair may occur. Depigmented body hair within vitiligo macules are considered as markers of poor repigmentation prognosis.

➢ **Clinical types of vitiligo**

Vitiligo	Subtype
Non segmental vitiligo (NSV)	Acrofacial Mucosal (more than one mucosal site) Generalized *(Vulgaris: multiple areas in symmetrical pattern)* Universal *(80--90% of BSA)* Mixed (associated with SV) Rare variants
Segmental vitiligo (SV)	Uni-, bi-, or pleurisegmental
Undetermined/unclassified vitiligo	Focal Mucosal

A- Non-segmental vitiligo : Clinically, NSV is characterized by depigmented macules that vary in size from a few to several centimeters in diameter, often involving both sides of the body with tendency toward symmetrical distribution. Contrary to SV, in NSV, body hairs are usually spared and remain pigmented, although hair depigmentation may occur with disease progression. Types :see above.

Rare variants:

- ✓ *Vitiligo punctuate(Guttate):* punctiform 1- to 1.5-mm macules.
- ✓ *Vitiligo minor*: The disease seems to be limited to dark-skinned individuals. The term 'minor' refers to the partial defect in pigmentation. The differential diagnosis from early stage cutaneous lymphoma is of primary importance, and repeated biopsies with molecular studies of clonality may be needed ***(Passeron & Ortonne, 2010).***
- ✓ *Follicular vitiligo:* primary involves the follicular reservoir with limited skin involvement.
- ✓ *Inflammatory Vitiligo* : The lesions could sometimes have a raised red border. A mild pruritus could be associated.
- ✓ *Multichrome Vitiligo* : This form of vitiligo is mostly seen in darker phototypes. Within a vitiligo lesion, areas of depigmentation coexist with hypopigmented areas and with normal color as in surrounding skin. In the hypopigmented area, a partial loss of melanocyte is observed Trichrome vitiligo is commonly used to describe this pattern, but various degrees of hypopigmentation can be observed leading to trichrome, quadrichrome, or pentachrome vitiligo
- ✓ *Occupational/contact vitiligo* :The terms 'contact' or 'occupational vitiligo' have been used to describe a distinct form of vitiligo induced exposure to certain chemicals phenols and catechols .

B- SEGMENTAL VITILIGO (SV): One or more white de-pigmented macules distributed on one side of the body, usually respecting the midline, early follicular involvement (leukotrichia), and rapid development over a few weeks or months, and overall protracted course.

Segmental Vitiligo (SV)	Nonsegmental Vitiligo (NSV)
- Often begins in childhood	- Can begin in childhood, but later onset is more common
- Has rapid onset and stabilizes	- Progressive, with flare-ups
- Involves hair compartement soon after onset	- Involves hair compartment in later stages
- Is usually not accompanied by other autoimmune disease	- Is often associated with personal or family history of autoimmunity
- Often occurs on the face	- Commonly occurs at sites sensitive to pressure and friction and prone to trauma
-Is usually responsive to autologous grafting, with stable repigmentation	- Frequently relapses in situ after autologous grafting

D- UNDTERMINED/UNCLASSIFIED VITILIGO

- *Focal vitiligo:* isolated hypopigmented lesion that does not fit a typical segmental distribution, and which has not evolved into NSV after a period of 1–2 yr.

- *Mucosal vitiligo.*

VITILIGO-ASSOCIATED COMORBIDITIES : Vitiligo is not only a disease of melanocytes of the skin. Human melanocytes are derived from the neural crest and are located on various parts of the body. Some authors underlines the fact that vitiligo is the skin manifestation of an internal disease.

1- Vitiligo and autoimmune disorders

Generalized vitiligo is frequently associated with other autoimmune diseases, particularly autoimmune thyroid diseases (Hashimoto's thyroiditis and Graves' disease) and ***antithyroid antibodies*** (30% مهمة جدا جدا والافضل تتعمل مع كل المرضى), rheumatoid arthritis, adult-onset type 1 diabetes mellitus, psoriasis, pernicious anemia, systemic lupus erythematosus, and Addison's disease.

2- Vitiligo and ocular diseases

The uveal tract and retinal pigment epithelium contain pigment cells. The most severe form of uveitis is seen in the Vogt-Koyanagi-Harada syndrome. This syndrome is characterized by vitiligo, uveitis, aseptic meningitis, dysacusis, tinnitus, poliosis, and alopecia.

Alezzandrini syndrome: includes facial vitiligo, poliosis, deafness, and unilateral visual changes. The affected eye has decreased visual acuity and an atrophic iris.

❖ **Histopathology:**

Microscopic examination of involved skin shows a complete absence of melanocytes in association with a total loss of epidermal pigmentation. Superficial perivascular and perifollicular lymphocytic infiltrates may be observed at the margin of vitiliginous lesions, consistent with a cell-mediated process destroying melanocytes. Degenerative changes have been documented in keratinocytes and melanocytes in both the border lesions and adjacent skin. Other documented changes include increased numbers of Langerhans cells, epidermal vacuolization, and thickening of the basement membrane. Loss of pigment and melanocytes in the epidermis is highlighted by Fontana-Masson staining and immunohistochemistry testing.

❖ **DIFFERENTIAL DIAGNOSIS OF VITILIGO**

i- Differential diagnosis of non-segmental vitiligo(NSV):

Diagnosis	Features
- Inherited or genetically induced hypomelanoses	
Piebaldism	White forelock, midline depigmentation of anterior body, bilateral shin depigmentation; autosomal dominance
Tuberous sclerosis	Small or larger (ash-leaf) white spots, seizures, typically later appearance of other cutaneous symptoms (e.g., shagreen patches, angiofibromas); autosomal dominance
Ito's hypomelanosis	Linear distribution, unilateral or bilateral pattern of hypopigmented streaks; sporadic; chromosomal or genetic mosaicism (involving blood or skin cells)
Waardenburg's syndrome	White forelock, hypertelorism, deafness (varies according to genotype); possible association with congenital megacolon (Hirschsprung's

	disease)
- Postinflammatory hypopigmentation: Occurs in inflammatory disorders accompanied by increased epidermal turnover (e.g., psoriasis, atopic dermatitis), in lichenoid–cytotoxic infiltration of epidermal basal layer (e.g., lichen planus, toxic drug reactions), and in scleroderma; clinically distinguished by identification of the primary skin disease (e.g., scalp or plaque psoriasis, flexural dermatitis for atopic dermatitis, scleroderma plaques), but may coexist with primary disease; in genital areas, lichen sclerosus may resemble vitiligo or be associated with true vitiligo; biopsy is useful in cases that are difficult to diagnose	
- Paramalignant hypomelanoses	
Mycosis fungoides	May present with skin depigmentation in dark-skinned patients; clinical diagnosis may be difficult in the absence of signs of inflammation and skin infiltration; biopsy results are diagnostic
Melanoma	Vitiligoid changes range from halo of depigmentation around a cutaneous melanoma (malignant Sutton's phenomenon) to more widespread vitiligoid changes; under Wood's lamp, the margins of such vitiligoid lesions are usually less distinct than in common vitiligo, and depigmentation is usually incomplete

- Parainfectious hypopigmentation	
Tinea versicolor	Can cause vitiligoid changes, generally after treatment in the absence of re-exposure to UV light; the distribution and shape of the lesions and the presence of scaling and yellow fluorescence of untreated lesions allow a definite diagnosis
Indeterminate leprosy	Manifested as hypochromic patches that are hypoesthetic to light touch
- Progressive macular hypomelanosis: Seen in young adults and frequently referred to as a recalcitrant pityriasis versicolor; white macules are present on the trunk, with more marked involvement on the lower back and axillae; Propionibacterium acnes is a suspected cause of depigmentation	
- Post-traumatic leukoderma: May occur after deep burns or scarring in which hair follicles are removed entirely or in which the bulge area containing melanocyte precursors is destroyed; can be difficult to distinguish from true vitiligo when scarring is not obvious; may also occur after toxic epidermal necrolysis	
-Occupational and drug-induced depigmentation	
Occupational	A subtype of vitiligo triggered by occupational exposure, which evolves from contact depigmentation (generally caused by a phenolic-catecholic derivative*) to a generalized phenomenon; may be difficult to distinguish from other cases of vitiligo
Drug-induced	Can result from use of systemic drugs (e.g., chloroquine, fluphenazine, physostigmine, imatinib); in rare cases topical imiquimod may also cause vitiligoid depigmentation

ii- Differential diagnosis of segmental vitiligo (SV):

- Nevus depigmentosus(ND): (Achromic Nevus)

Nevus depigmentosus is a congenital pigmentary disorder. The disease is primarily limited to the skin though there are reports of association of neurological abnormalities and limb hypertrophy. The commonly used clinical diagnostic criteria are as follows:

- Leukoderma present at birth or of an early onset.
- No alteration in the distribution of leukoderma throughout life.
- No alteration in texture or change in sensation in the affected area.
- Absence of hyperpigmented border.

DD
1. at or shortly after birth
2. Stable
3. W. L 4. Bio

Nevus depigmentosus is generally classified as isolated, segmental, and whorled types. Wood's lamp examination shows an "off-white accentuation" in ND as compared to the chalky white accentuation in the case of vitiligo. The lesion usually contains a normal or subnormal number of melanocytes compared with control perilesional skin, but the production of melanin pigment is reduced. Sun exposure may attenuate the difference in pigmentation from normal skin. In difficult cases, a biopsy is needed to differentiate naevus depigmentosus from SV

- *Hypomelanosis of Ito:* is a rare neurocutaneous syndrome characterized by hypopigmented skin lesions with a peculiar pattern of streaks, whorls, swirls, and patches. The associated systemic abnormalities predominantly affect the nervous and musculoskeletal system and less commonly gastrointestinal, renal, and cardiac systems.

A solitary white macule or several white to off-white macules often present a challenge because they may be the presenting stage in the evolution of any of the processes listed above. In some instances, a biopsy may be helpful, but standard histologic studies cannot distinguish a vitiligo macule from one of chemical leukoderma, piebaldism, or Waardenburg's syndrome . Biopsy is useful to establish diagnoses such as lupus erythematosus, leprosy, and tinea versicolor. The presence of melanin or melanocytes in a biopsy cannot be assumed to exclude a diagnosis of vitiligo because trichrome vitiligo, perilesional skin, and repigmenting macules of vitiligo also demonstrate melanocytes.

Nævus depig
Failure of Melanosome transfere

H/P edge
- degenerate Kc, Mc
- depigmentation (Center)
- infiam infilt
- ↑ Lcs

TREATMENT OF VITILIGO

➢ Introduction

Treatment of vitiligo is aimed at stopping the disease progression and restoring the loss of melanocytes in the lesions. No single therapy for vitiligo produces predictably good results in all patients; the response to therapy is highly variable.

Recovery of vitiligo is initiated by proliferation, migration and melanogenesis of melanocytes still present in the hair follicle units (perifollicular pattern of repigmentation), in the margins of vitiligo lesions or spared epidermal melanocytes within the achromic lesions.

In general, patients with a family history of vitiligo, mucosal involvement, a positive Koebner response, and the NSV subtype of vitiligo tend to have progression of their condition in the absence of therapy. The best response to treatment is seen in younger patients, disease of recent onset, darker skin types, and in lesions on the face, neck, and trunk. Distal extremities tend to be extremely refractory to non-surgical modalities.

❖ Treatment of vitiligo can be classified into :

A- Medical treatment
B- Photo(chemo)therapy
C- Laser therapy
D- Antioxidants
E- Surgical Treatment
F- Depigmentation Therapy
G- Camouflage
H- New concepts in treating vitiligo

➢ MEDICAL THERAPY

1- Systemic corticosteroids (CSs): Systemic steroids can arrest the activity of the disease, but are not effective in repigmenting stable vitiligo. Oral minipulse therapy of betamethasone/dexamethasone 2.5-10mg on 2 consecutive days per week for 3-6 months has been pioneered in India. . Moreover, side-effects associated with long-term use of daily systemic corticosteroids contraindicate their common use .

2- Topical corticosteroids: Topical steroids are the most clinically effective choice for topical therapy and often first-line therapy, especially in children or for localized disease. Moderately potent to potent topical corticosteroids are used. However, vitiligo requires prolonged use of these agents, often much longer than the usual "safe" recommended periods of use for inflammatory dermatoses. This results in significant, therapy-limiting side-effects like atrophy, hypertrichosis and peri-lesional hypopigmention.

Doses of 50 gm or less per week of clobetasol propionate 0.05% during a period of 12 weeks are safe on adult vitiligo patients, although local side effects are possible. Topical all-trans-retinoic acid (tretinoin) prevents skin atrophy induced by long-term use of topical corticosteroids, without abrogating their anti-inflammatory effects.

3- Topical calcineurin inhibitors (TCI): TCI (tacrolimus & pimecrolimus) can be to selected areas, in particular the head and neck region to avoid SE of topical Cs. Compared to topical corticosteroids, TCI produce slightly inferior to equivalent repigmentation rates, but the effect occurs earlier in the course of treatment.

4- Topical vitamin D_3 analogs : Topical calcipotriene (a vitamin D_3 analogue) is sometimes used for localized disease, but trials have indicated that it has limited or no effect when used alone and that it results in at most a minor increase in repigmentation when used in combination with ultraviolet radiation or topical corticosteroids. Calcipotriene 0.005%/betamethasone dipropionate 0.05%- 0.064% ointment is effective and well tolerated in the treatment of patients with vitiligo. Adult and pediatric facial vitiligo patients may see repigmentation as early as 2 months after initiation of therapy.

➢ PHOTO(CHEMO)THERAPY

Ultraviolet light has been used to treat patients with vitiligo since the 1800s. The exact mechanism of action is unknown: it is believed to have both immunosuppressive and melanocyte stimulatory effects (migration and proliferation).

Phototherapy induces a predominantly perifollicular pattern of repigmentation, whereas topical agents exhibit a diffuse type, acting synergistically when combined.

1- Ultraviolet A (UVA) Phototherapy

✓ *Systemic (oral)PUVA:* PUVA is approved by the Food and Drug Administration (FDA) for the treatment of vitiligo. Psoralen photochemotherapy involves the use of psoralens combined with UVA light. For oral PUVA, 8-methoxypsoralen (8-MOP:0.6–0.8 mg/kg), 5-methoxypsoralen (5-MOP; 1.2–1.8 mg/ kg) or 3 trimethylpsoralen (0.6 mg/ kg) is given orally 1–3 h before exposure to UVA. The best results from PUVA can be obtained on the face, trunk, and proximal parts of the extremities. However, 2-3 treatments per week for many months are required.

✓ *Topical PUVA:* a thin coat of 8-MOP cream or ointment at very low concentration (0·001%) should be applied 30 min before UVA exposure. The main disadvantages are severe blistering reactions, perilesional hyperpigmentation and lack of effectiveness in limiting the progression of actively spreading vitiligo.

✓ *Khellin UVA (KUVA):* Another photochemotherapy regimen, KUVA, consists of khellin as the photosensitizer (furanochrome extracted of the plant Amni visnaga and UVA). KUVA's lack of phototoxicity makes it safe for use as a home treatment or treatment with natural sunlight, even in a daily regimen. It is also less mutagenic than psoralens and it promotes less darkening of normal skin.

2- Narrow-band ultraviolet B (NB-UVB):

NB-UVB is indicated for generalized NSV. Total body treatment is suggested for lesions involving more than 15–20% of the body area. Total NB-UVB has also

been considered as treatment for active spreading vitiligo, even if limited supportive data are available. Many therapists tend to stop irradiation if no repigmentation occurs within the first 3 months of treatment or in case of unsatisfactory response (< 25% repigmentation) after 6 months of treatment. Phototherapy is usually continued as long as there is ongoing repigmentation or over a maximum period of 1 or 2 years. Maintenance irradiation is not recommended, but regular follow-up examinations are suggested for detecting relapse.

Compared to PUVA, NB-UVB is found to be superior to PUVA due to various reasons including better repigmentation, stabilization and color match with natural skin, a better safety profile as it maximizes the delivery of narrow-band UVB radiation in the range of 312-313 nm which is the most beneficial of the UV spectrum, while minimizing exposure to superfluous UV radiation thereby considerably decreasing the risk of severe burning or pathogenic exposure to UV in harmful ranges. It also avoids the adverse side effects of the psoralens used in conventional PUVA therapy. As UVB treatment requires no supplemental drugs and is considered to be effective and safe in children and pregnant women. There is no need for post treatment eye protection as should be done with PUVA.

- **LASER THERAPY:** . Excimer laser is relatively safe and effective for localized disease. UV-sensitive areas respond best as well as a short duration of the disease. More frequent treatments achieve better results. Compared to other treatment modalities, the excimer laser most likely constitutes the treatment of choice for localized vitiligo.

- **ANTIOXIDANTS:** Pseudocatalase, vitamin E, vitamin C, ubiquinone, lipoic acid, *Polypodium leucotomos*, catalase/superoxide dismutase combination, and *Ginkgo biloba* are antioxidants that have been used alone or, more frequently, in combination with phototherapy. The administration of antioxidants during or before phototherapy aims to counteract the oxidative stress induced by UV radiation itself, increasing its effectiveness.

Catalase and superoxide dismutase are enzymes with antioxidant properties. They are available in a combination topical medication marketed outside of North America as *Vitix*.

- **SURGICAL REPIGMENTATION THERAPY**

Surgical alternatives exist for the treatment of vitiligo; however, because of the time-consuming nature of surgical therapies, these treatment regimens are limited to segmental or localized vitiligo. Unilateral (segmental) vitiligo has been shown as the most stable form, responding well to surgical interventions in numerous studies. Such areas as dorsal fingers, ankles, forehead, and hairline tend to not repigment well. Patients who have small areas of vitiligo with stable activity are candidates for surgical transplants. The most important factors indicating stability are as follows:

- No progression of lesions for at least 2 years.
- Spontaneous repigmentation indicates vitiligo inactivity.

- A positive minigrafting test disclosing repigmentation at 4-5 minigrafts, which, to date, is the most accurate evidence of vitiligo stability.
- Absence of new koebnerization, including the donor site for the minigrafting test.
- Unilateral vitiligo is the most stable form of vitiligo (SV)

- Types of surgical therapy:

I- Tissue Grafting:

- *Minigrafting (punch Grafting):* In this method, grafts are harvested with the help of biopsy punch, preferably from the gluteal region, and fixed into the pits created by a similar instrument to the recipient area. They are secured with micropore tape or steri strips. Dressing is removed after 7-14 days.

- *Split thickness skin grafting:* This method uses skin grafts harvested with either a hand-held Humpy's knife and placed directly on the recipient area prepared by laser ablation or motorized dermabrasion. They are secured with surgical dressing, which is removed after 1 week.
- *Suction blister grafting:* Epidermal grafting involves obtaining pure viable epidermis-bearing melanocytes in the form of blisters by applying negative pressure (300-500 mmHg) to the normally pigmented skin. The grafts thus obtained are transferred to the denuded recipient sites. Suction Blistering Epidermal Graft is one of the most efficient and successful surgical modalities.

II- Cellular Grafting (Noncultured & Cultured Techniques):

These techniques use separated cells in the form of suspension. These cellular suspensions are transplanted as noncultured suspension or after culturing them *in vitro* on to the recipient area. The major advantage of these suspension and culturing techniques is that, they permit treatment of affected skin manifold larger than the donor area *(van Geel et al., 2011).*

- *Noncultured melanocyte-keratinocyte transplantation* : After the achromic epidermis is removed, an epidermal suspension with melanocytes and keratinocytes previously prepared by trypsinization of normally pigmented donor skin is spread onto the denuded area and immediately covered with nonadherent dressings
- *Cultured-melanocyte transplantation:* Depigmented skin is removed using liquid nitrogen, superficial dermabrasion, thermosurgery, or carbon dioxide lasers; very thin sheets of cultured epidermis are grafted or suspensions are spread onto the denuded surface.
- Stem Cells: Grafting of Stem / Reservoir MCs in Pulge area of ORS of HF

- DEPIGMENTATION THERAPY

This treatment should generally be reserved for adults who have severe vitiligo with > 50% depigmentation or extensive depigmentation on the face or hands that cannot be repigmented or for adults who choose not to seek repigmentation and can accept the permanence of never being able to tan.

Monobenzyl ether of hydroquinone (MBEH) is the mainstay and FDA approved to depigment and is associated with local side effects and risk of repigmentation. Other agents which are also used are 4-methoxy phenol and 88% phenol. Physical therapies for depigmentation include Q-switched ruby and alexandrite lasers and cryotherapy. Second-line agents which can be explored for depigmentation include imatinib mesylate, imiquimod, and diphencyprone.

- MBEH
- Phenol

- **CAMOUFLAGE** ;There is a wide choice of self-tanning agents, stains, dyes, whitening lotions, tinted cover creams, compact, liquid and stick foundations, fixing powders, fixing sprays, cleansers, semipermanent and permanent tattoos, and dyes for pigmenting facial and scalp white hairs. Permanent camouflage, micropigmentation and tattoos should be considered with particular caution, due to the unpredictable course of the vitiligo.

❖ CHOICE OF TREATMENT

Each therapeutic modality should be tried for a sufficient period of time as initiation of pigmentation varies and is in general rather slow. An effective therapy should be continued as long as there is improvement or the lesions completely repigment.

other lines :-

- 5 Fu + Dermabrasion.
- PRP

5) Vogt Koyanagi - Harada
. Poliosis & Alopecia
[. Vitiligo. (Generalized)
. Uveitis
[. Meningitis
. otic (dysacusia) & Tinnitus

Vitiligo

↓

has 5 Syndromes. "Related"

[٥ آخوات]

① Piebaldism (Partial Albinism) (AD); KIT proto-onco gene Mutation.

- : at birth & doesn't ↑ in extension (≠ Vitiligo)
- . White forelock (△ or ○ shape).
- . Vitiligo like amelanotic macules — containing few hyperpigmented macules.

(at) / Central ant. Trunk. — mid extremities. — Central forhead

. Spare post midline

AET: ↓ MC expression of "stem cell factor" Receptor ⟶ failed migration from dorsal aspect to ventral aspect during embroynic development ⟶ Ventral surfaces only affected ← Abd. Forehead Volar arms & Legs.

② Woolf's Synd : As Piebaldism + deafness

③ Waardenburg's Synd: (AD)

AS Woolf's + Eye:
- Heterochromia Iridis.
- Lat. displaced inner canthi (ⓔ NL inter pupillary discs) (Dystopia Canthorum);
- Confluent Eye brow. (Synophrys)
- Broad Nasal Root
- Deafness.

Type	
WS1: Classic	WS3: limb defect
WS2: No Dystopia Canthorum	WS4: ass Hirschsprung

④ Alezzandrini Synd

. unilat. Retinitis ⟶ then
. Ipsilat. Vitiligo of Face
. Ipsilat. poliosis
. + Deafness

Neutrophilic [illegible]

أهم التعريف

(Def.) Inflammatory dermatoses ch- histopathologically be predominant Neutrophilic Infilt. in absence of ⟨ Infection & Vasculitis
show prompt response to Cs.

Epid.

- pustular ps.
- AGEP

- SCPD
- IgA pemphigus < نوعين

- Infantile Acropustulosis
- Transient Neonatal Pustular Melanosis. (TNPM)

- Keratoderma Blenorrhagicum.
- Amicrobial pustulosis of folds.
  (♀ ē chr. pustulosis of: Folds, EAC, Scalp + CTDs.)

Dermal

with Vasculitis

يعتبر حالة Vasculitis

1. Small V V.
2. Med. V V
3. large V V

"Neutrophilic urticaria" كتنبى

without Vasculitis

"أهم ND"

- Sweet Synd.
- PG
- Behcet
- BADAS

- Neutrophilic Eccrine Hidradenitis
- Rheumatoid Neutrophilic dermatitis
- SAPHO synd
- Neutrophilic urticaria ??
- Still's dis
- periodic Fever synds.

→ All HL

3 Neut ⟨ urtic, Eccr, Rheum.

- Bullous dis:
  - DH
  - LAD
  - BSLE
  - EBA (inflammatory type).

+/- Vasculitis

- Pustular Vasculitis of dorsal Hands.

Acute Febrile Neutrophilic dermatosis

سؤال امتحان

. Bulgarian
. Andr.
. Qassim
. عام

(Sweet Syndrome)

(5)

. Def: Commonest ND (prototype of all ND).

. Epidemiology : . Age : . Typically → 30 - 50 Y.
. Som cases → neonates ≃ 5 days.

. Sex [1] Classical Type → M : F = 1 : 4 [2] Mg & Childhood Type : M = F

Criteria حفظ جيدا ولو الامتحان طالب CIP زود عليها

زيادات :

A. Systemic Prodroma
- FAHM
- Arthralgia
- Myalgia
- CNS < Psychosis, Migraine, Seizures
- Pulm. <
- GIT, Bone & renal.

B. Cut. زيادات
oral & ocular Inflamm
↓ ulcerat (more ē Mg)

. Course : Exacerb. & remission.
. Recurrence : 30 - 50 % (classic.) (Mg)
. No Scarring

حفظ جيدا (JAAD)

Major Criteria < Clinical, HP

(Onset) 1. Abrupt onset of : < Painful or Tender < Erythematous or Violaceous
< Nodules or plaques ± ē < Vesicles or pustules or Bullae. Pseudo Vesicles (mamillated Edema). Annular. 2 Targetoid.

(Infil.) 2. predominantly dermal Neutrophilic infilt. (without شرط) LCV.

Minor Criteria

1. أو معاه : تسبقه < inf. / vaccinat.
- Inf. ← URTI, HCV, HBV, TB.
- Drug → (Doxy-retinoid, GCSF, Azith.).
- Mg — الأشهر . Leuk. (AML) (10-20%)
- IBD
- AICTD
- Pregnancy

. URTI, (Strept.)
. GIT inf., or (Yersiniosis)
. Vaccinat. (BCG)

2. Fever > 38°C & Malaise.

3. Lab Findings : (≥ 3)
- ESR > 20.
- +ve CRP.
- Leukocytosis > 8000.
- > 70 % Neutrophilia

4. Excellent response to CS (or) KI.

For diagnosis : 2 Major + 2 Minor.

Treatment

Cs ← العلاج الاساسي (1)

(0.5-1 mg/kg/d For 4-6 ws)

(2) البدائل:

- KI (900 mg/d)
- Dapsone (100-200 mg/d)
- Colchicine (1.5 mg/d)
- NSAIDs; Indomethacin.

.. Types of Sweet:

1. Classical (Idiopathic) (70%)
2. Localized: ← Face, dorsal Hands (NVDH)
3. Mg. associated (10%)
4. Inflamm. dis. Associated (Infl AICTDs)
5. Pregnancy ass.

ولكن تذكر أن هذا المرض:

1. Bg condion; If untreated it well remains ws-ms (بوزنيا ↓ (5-12 ws))
2. Cut lesions → involute Eout scarring
3. Recurrence: (جع الربيع الخريف)
   - ē classical cases → 30% (Even ē tt)
   - Mg ass. " → 50%
4. Treat URTI

Mg Sweet ?? سؤال امتحان

NB:

Characteristic features of malignancy associated Sweet's syndrome

1. NO < sex predilection (M=F), URTI
2. Blood: Anemia
   - Thrombocytopenia
   - (-ve) Neutrophilia in >50%
3. lesion: appear Before Mg (60%)
   - Severe wide spread.
   - Bullous or ulcerative & oral mm. affect
   - Highly recurrent (≥50%) & often herald Tm relapse.

Acute febrile neutrophilic dermatosis is a misnomer ?

- Chronic recurrent forms exist.
- Fever and neutrophilia are variable features.
- Extracutaneous manifestations are common.

DD بوزنيا 383

Pyoderma Gangrenosum

Etiopath. = Associate
Criteria For Dx
Types
HP & TTT

For diagnosis: 2Major+2Minor

Major criteria (both required)
1. Rapid (usually > 1 cm/day) progression of painful necrolytic ulceration with an irregular, undermined, violaceous border, usually with a preceding papule, pustule or bulla, and pain out of proportion to the size of the ulcerated area.
2. Exclusion of other causes of ulceration.

Minor criteria (at least 2 required)
1. (a) history of pathergy, or (b) presence of cribriform scarring.
2. Presence of a disease known to be associated with PG (IBD, polyarthritis, myelodysplasia, leukaemia, monoclonal gammopathy).
3. Appropriate histopathological findings.
4. Rapid response to oral corticosteroid therapy (usually interpreted as at least 50% reduction in size using 1-2 mg/kg/day).

Classification of PG

Morphologically

Ulcerative (Typical)	Bullous	Pustular	Vegetative
Frequent	Frequent	Frequent	Uncommon
Arthritis, IBD, monoclonal gammopathy	Hematologic dyscrasias/ Malignancy	IBD	No systemic associations/ Chronic renal impairment
Lower limbs (Prefibial)	Upper limbs	Face and trunk	Trunk

- IBD: 20-30
- Arthritis: RA · ay sero-ve (20%)
- IgA: 15% (plasma cell dyscrasia)

Clinical types	Histopathology
Ulcerative [Figure 5]	Edema, neutrophilia Secondary lymphocytic vasculitis
Bullous	Epidermal necrosis with neutrophilia, subepidermal bulla
Pustular	Epidermal and dermal neutrophilia
Vegetative	Neutrophilic and eosinophilic and histiocytic mixed infiltrate. Intra- and subepidermal granuloma formation

Treatment

Best is Cs (Topical & Syst.)

others
- IL Cs
- Tacrolimus
- Dapsone
- Lamprene
- SulfaSalaZn
- MTX
- Ciclosporin
- Thalidomide

Associations → 7
- 4: IBD, Arthritis, IgA gamm, Ma (lymphoma)
- 3: PAPA: P Prog. Arthritis, PG & Acne.
  PASH: PG, Acne, S. Hidradenitis.
  PAPASH: PAPA + Supp. Hidradenitis.

[تحفظ الجداول جيدا ثم بعد ذلك يقرأ التفاصيل]

Behcet Disease (Oculo-oral genital Synd.)

-Diagnostic criteria according to ISG (International study group for Behçet's Disease .1990)

مهم جدا

Criterion	Required features
Recurrent oral ulceration	Minor aphthous, major aphthous, or herpetiform ulceration observed by physician or patient, which recurred at least 3 times in one 12-month period
Plus any two of the following:	
Recurrent genital ulceration	Aphthous ulceration or scarring, observed by physician or patient
Eye lesions	Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination; or Retinal vasculitis observed by ophthalmologist
Skin lesions	Erythema nodosum observed by physician or patient, pseudofolliculitis, or papulopustular lesions; or Acneiform nodules observed by physician in postadolescent patients not on corticosteroid treatment
Positive pathergy test	Read by physician at 24-48 h.

مهم جدا 2- "لا حدث"

International criteria for the diagnosis of Adamantiades-Behçet disease (2014) (9)

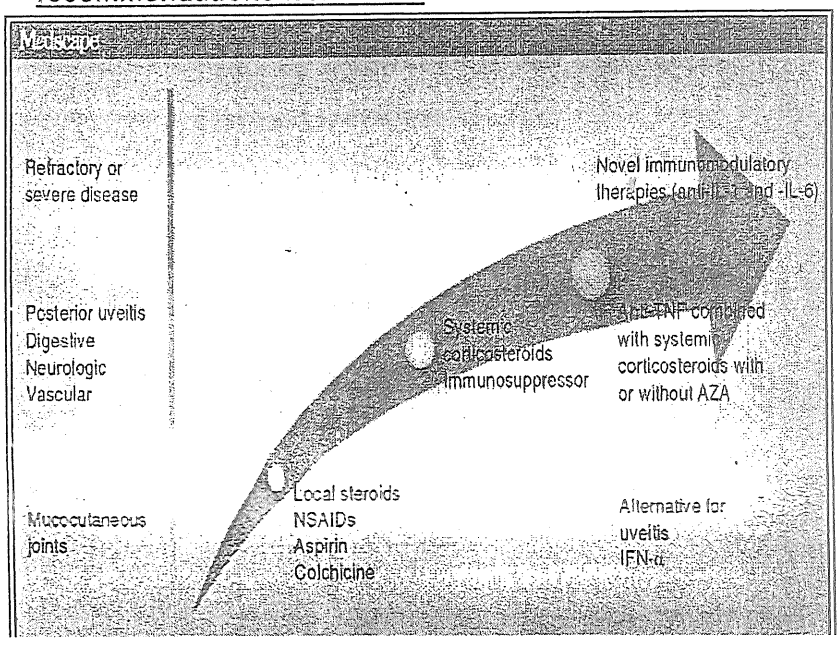
Recurrent oral aphthous ulcers	2
Skin lesions (papulopustules, erythema nodosum, thrombophlebitis)	1
Vascular involvement (arterial or venous thromboses, aneurysms)	1
Recurrent genital aphthous ulcers	2
Ocular involvement (hypopyon-iritis, uveitis)	2
CNS involvement (Meningo encephalitis / Nerve paralysis)	1
Positive pathergy test	1

Adamantiades-Behçet disease: 4 or more points

سبب الوفاة

- Etiopathogenesis of BD
  1. Genetic: HLA5 → B51, B27
  2. Immunologic: Type III reacta (Immune Complex)
  3. Inf.: HSV, HCV, Strep
- Age: 20-35
- Sex: M > F.

- Lines of TTT : According toThe European League Against Rheuma recommendations from 2008.



mild

Therapeutic ladder for complex aphthosis Behçet's disease

Complex aphthosis / mucocutaneous disease

- Topical@ intralesional corticosteroids.
- Colchicine
- Dapsone
- Combination of the above

Severe mucocutaneous disease (Eye)

- Thalidomide
- Low-dose methotrexate (7.5-20 mg/wk).
- Prednisone
- Interferon alpha

Severe ocular & systemic disease

- Prednisone
- Azathioprine (1-2 mg/kg/day)
- Cyclophosphamide
- Chlorambucil
- Cyclosporine (10 mg/day)

Cut.

Eye
Joint
CNS
Others.

C/P of BD (التفصيل)

1. Recurrent oral ulcers:

Recurrent يعني ايه !! → recur ≥ 3 times / Y (Either reported by patient or reliably physician).

- usually: painful.
- Types.

قرح فم متكررة مشابهة تماما لقرح الفم العادية

2	Minor	→ 1-5, small (< 10 mm) Moderately painful resolve in "4-14 d's" without scar (scaring only in 6%)
6	Major	→ 1-10 large (10-30 mm) Very painful persist up to 6 ws → scar (60%) High incid. of Antimucosal Abs.
4	Herpetiform	→ Recurrent crops of as many as 10-100 small (1-3 mm) painful ulcers. Heal: up to 4 ws. Recurr in 3d Low incid. of Antimucosal Abs

2. Recurrent Genital ulcers:

painful
- ♂: Scrotal > penile
- ♀: vulva, vagina, Cx.

3 Ocular

- Retinitis & Post Uveitis (...)
- A leading cause of morbidity d.t blindness.

4 other skin lesions → الجدول مهم

5 Pathergy test (امتحان)

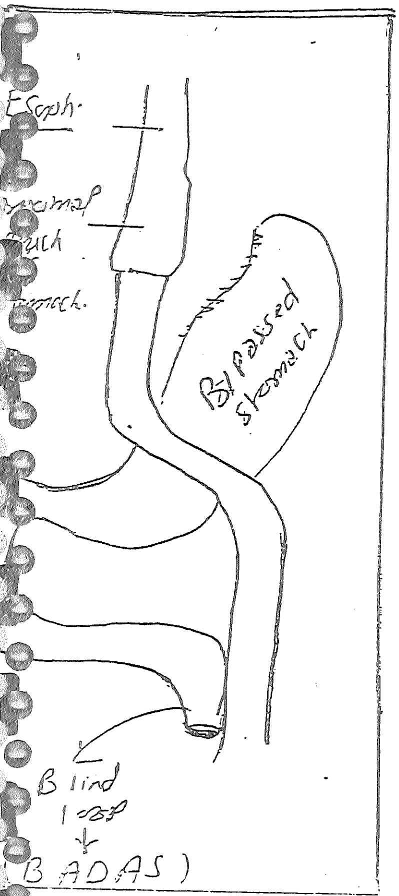
- Def. Hypersensitivity test (which) demonstrate ↑ Neutrophil chemotaxis at site of Trauma. (..... Koebner phenomena ( ))
- Method:
  - Needle prick of ID injection of 0.1 ml saline or histamine —1-2 ds→ Erythematous papule or sterile pustule (> 2mm)
- Results: may be +ve or -ve, if -ve → repeat at 2-5 points before results.

6 Systemic manifs

- CNS < Meningoencephalitis, Nerve paralysis
- Vascular (large Vs) < Thrombosis, Aneurysm → Hemoptysis
- GIT
- Joint.

Bowel associated Dermatosis Arthritis Syndrome (BADAS) (66)

(Bowel by pass Synd)



Roux-en-Y Gastric By pass operat°

①. By-pass operat° to Create blind loop as:

- . Jejunoileal by-pass Surgery
- . Gastric by pass "

② Bilio pancreatic diversion

③. IBD

④ Diverticulitis.

↓

Bacterial over growth in the blind loop → release of Bacteria Ags (as peptidoglycans) → Immune Complex formation → deposition in Skin & Joint.

↓ (1-6 ys)

Manifs of BADAS:

A. Cut. manifs. (Dermatosis = ND):

[1]. Usually: Erythematous macules → papules → purpuric vesiculopustules (within 48 hrs)

Common sites: Extremities & trunk.

[2] Other lesions: Erythematous S.C Nodules ± :

EN or Nodular non-suppurative panniculitis

- Nodular non supp. panniculitis
- . Scarring (depressed)
- . lobular
- . at legs, buttocks & abd.

DD

[B] Arthritis

[C] Nutritional deficiency

Neutrophilic Dermatosis (Pustular Vasculitis) of dorsal Hand

. Some Consider it as a localized variant of Sweet Syndrome.

. C/P Edematous ulcerative or pustular Nodules & plaques at dorsal Hands.

. Path. : as Sweet but there may be LCV.

. Ht : as Sweet.

.Neutrophilic Eccrine Hidradenitis

def. ND Ch BY inflamm. of Eccrine Sweat gland.

C/P : غالباً تحصل بعد جلسة كيماوى
وخصوصاً Cytarabin) مبشرة ا لـ ٢ م الثار
علاج حالات الـ Leukemia & Lymphoma
وغالبا بلاقى المريض منه Neutropenia.

. lesion . Erythematous, Edematous, papules, plaques, Purpura & pustules located
Acral
at . Face → (periorbital) عين
. Palms
. Extremities.

. There may be fever.

. Ht → . NSAIDs
. Dapsone
. Cs.

Extracut ND (Medscape.com → next).

NB: on Behcet dis (BD)

- Histopathology
  - Early: Neutrophilic Vascular Reac
  - Late: Lymphocytic Vasculitis.
  - According to Chapill HCC (2012) → Variable Vasculitis

- Behcet [DDs اللي ٣ إخوات]
  1. RAS: Recurrent Aphthus stomatitis.
  2. Complex Aphthosis
  3. MAGIC Synd: Mouth & genital ulcers with Inflammed Cartilage.

Complex Aphthosis

- def 3 ← recurrent oral ulcers
  - " genital "
  - No systemic manifs of BD
- Controversy: is it early BD or Forme fruste.

(New Criteria of BD) على حسب الـ

Complex Aph. لا يوجد حاجة أسمها

[BD هي تعتبر]

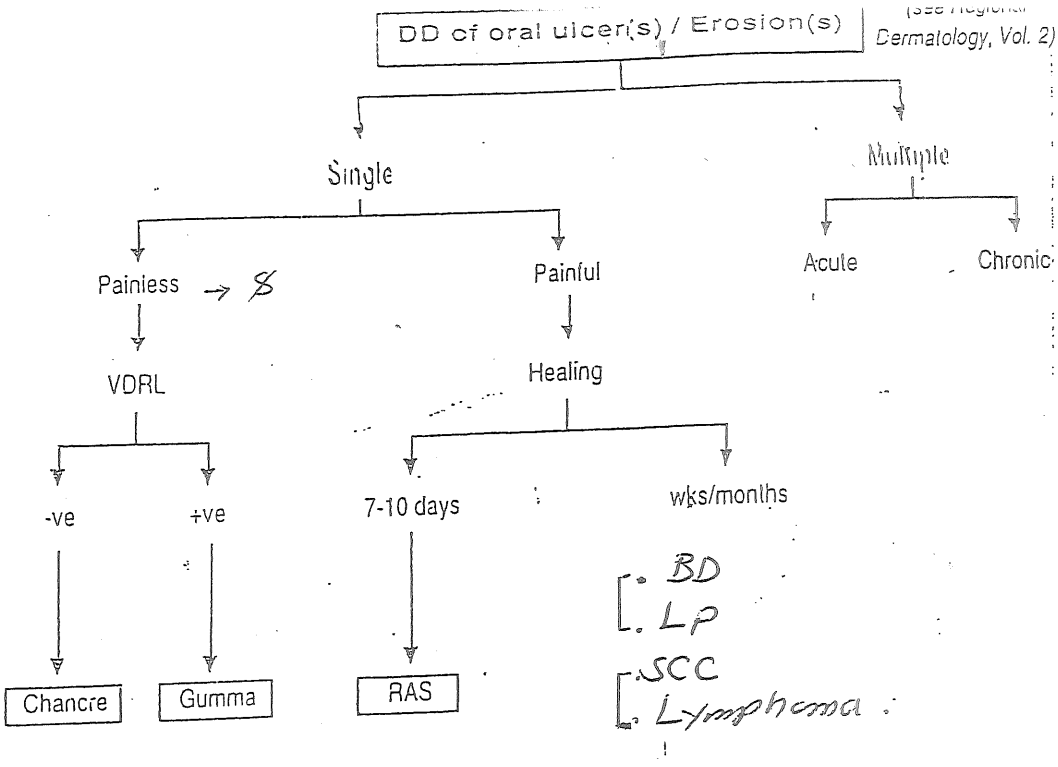
RAS = Recurrent Aphthus stomatitis

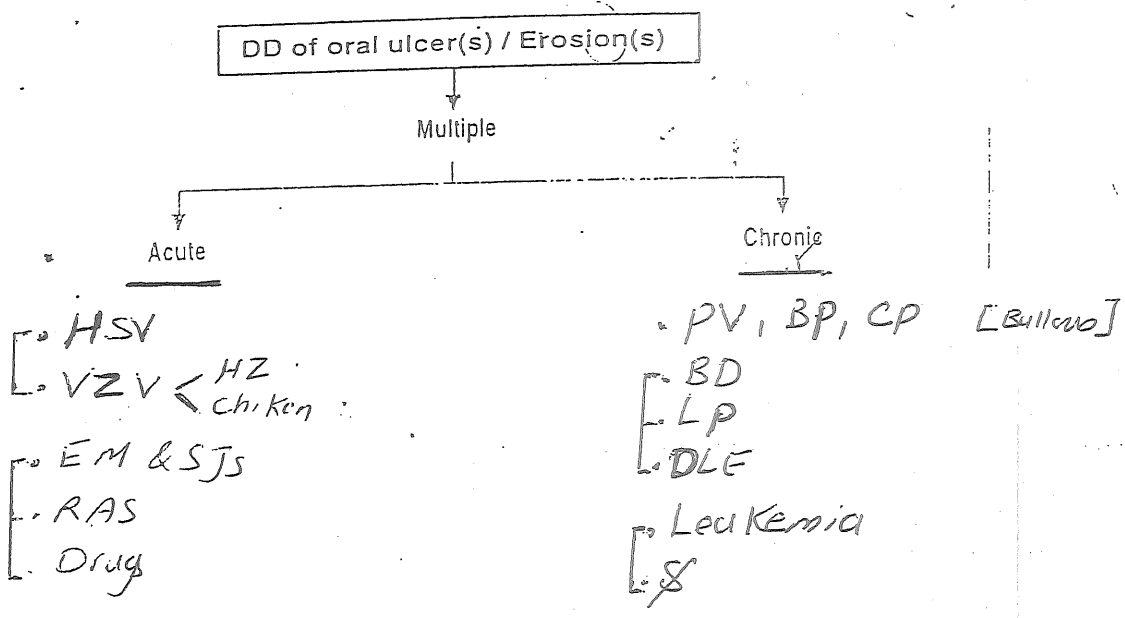
- Commonest ulcerative dis. of oral cavity (20% of populat)
- Predisposing Factors:
  (1) BD (2) Malabsorptn ← Coeliac / Crohn's
  (3) Stress (4) Cessat of smoking
  (5) Trauma & Certain Foods
  (6) Inf. ← Strept. / H. pylori
  (7) Idiopathic

Tt
① Topical:
- Tetracycline Mouth Wash
- Anaesthetic
- Cs

② Systemic
- Dapsone
- Colchicine
- Thalidomide
- Azathioprine.

- Types of ulcers: minor (80%), Major (10%), Herpetiform (10%)





. Complex Aphthosis: ≥ 3 oral ulcers + Genital ulcers but No systemic Manifs. of BD

. Oculomucocut Synd. (DD of BD)

. BD (Behcet)
. EM
. Sweet
. Reiters

. PV
. CP
. ⊗
. HSV
. LE.
. MCTD.

احمد ان

Eosinophilic dermatoses

(75)

→ (discoses ch BY Predominant Eosinophilic infilt.) (± peripheral Blood Eosinophilia) as evident of Eos. degran.

.3 4.FV → (1.) Well's synd
(2.) Granuloma Faciale
(3) Hypereosinophilic synd.

• Well's Syd (Eosinophilic cellulitis)

• Chr. recurrent Cut. disorder CK < Clinically by: Cellulitis like rash / pathologically by: Flame figures.

• Etiopath.: (1). Arthropod bites
(2). Infect / Infest. → Viruses / Tinea / Toxocara canis ✓
(3). Myeloprolif.

• Epidemiology: Adults, without predilect.

• C/P. itchy or burning, indurated Erythematous Nodules & plaques (cellulitis like) —4-8 w→ Faint-pink, brown or slate gray pigm. on limbs → recurrence.

• There may be < FAHM, Eosinophilia. / Clinically Varieties: papules, vesiculobullous & Annular.

(path) Deep dermal (± SC or fascial) Eosinophilic infilt.
+
Flame figures [Collagen coated by Eosinophilic granular proteins].

(Lab) • Blood < ↑Eos. / ↑Eos. Cationic ptn. (ECP) / ↑IL5

• Toxocara canis (Ø): < Stool / IgE / antibodies.

DD < (Clinically) → See pseudocellulitis & cellulitis.
(Path.) → Causes of Flame figure: Arthropod bite, scabies, Eczema, Drug Erupt. & Mastocytomas, Sweet.

Tt → الأرخص Cs: 10-80 mg/d tapered over 1m. → dramatic Response
→ Others. Topical Cs, Dapsone, Minocycline, Griseofulvin & Antihistamines.

Granuloma Faciale (GF) (76)

(± self limiting)

Def: Chr., Bg, Idiopathic skin disorder Cl By

Single or Multiple red-brown cut. Nodules on face.

Etiopathog.: ??

Epidemiology: Middle age ♂ > ♀

Clp: . Single, Asympt., Smooth red-brown or Violaceous plaque on Face ± prominent follicular opening.

. Varieties < Multiple lesions.
papular lesions.
Extrafacial GF.
Nasal involvement (Eosinophilic angiocentric Fibrosis)

Course: (Vg) Associated Systemic Manifs.
(±) resolve Spont.

Path.:
. diffuse Mixed dermal Infilt. < E., N., L.
. LCV (±)
. Grenz Zone.

DIF: +ve deposition at Vs. wall < IgG, IgM, C3.

DD: (1) SL. (2) Sarcoidosis. (3) Granulomatous vasculitis over joints < Neutrophil. (LCV, No Grenz, Epid change)
(4) EED - (difficult to Diff. from Extrafacial GF; by

Rx (often resistant)

1st line: IL Cs

2nd line: . Dapsone
. Clofazimine
. Tacrolimus
. PUVA

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Hypereosinophilic Synd (HES)

(77)

Diagnostic Criteria:

1. peripheral Blood Eosinophilia > 1500 /ul for > 6ms (or < 6ms but ± evidence of organ involvement).

2. Absence of other cause of Eosinophilia e.g. (Cyto)

3. Evidence of organ involvement (Thus excluding By Eosinophilia)

Types 1. Myeloproliferative.

2: Lymphoproliferative..

Mucakdtaneous lesions

(30% of cases)

. pruritic Erythematous papules or Nodules.

. Urticaria & Angiodema

. Mucosal Ulcure

Cause of death CHF.

(H): . Cs

. Imatinib